



CCM2 gene

CCM2 scaffolding protein

Normal Function

The CCM2 gene provides instructions for making a protein called malcavernin, which strengthens the interactions between cells that form blood vessels and limits leakage from the vessels. Malcavernin interacts with a number of other proteins to form a complex that is found in the junctions that connect neighboring cells. As part of this complex, malcavernin helps turn off (suppress) a signaling molecule known as RhoA-GTPase. This molecule plays a role in regulating the actin cytoskeleton, which is a network of fibers that makes up the cell's structural framework. When turned on, RhoA-GTPase stimulates the formation of actin fibers, which has been linked to weakened junctions between cells and increased leakage from blood vessels.

Malcavernin is also involved in a process called angiogenesis, which is the formation of new blood vessels.

Health Conditions Related to Genetic Changes

cerebral cavernous malformation

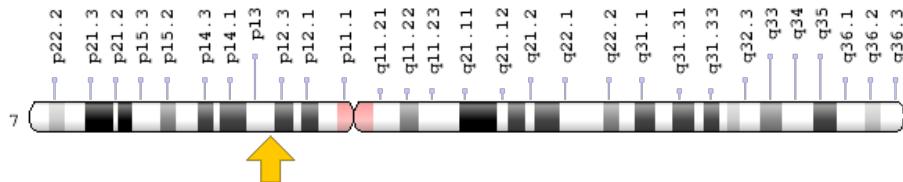
Dozens of mutations in the CCM2 gene have been identified in families with cerebral cavernous malformations, which are collections of blood vessels in the brain that are weak and prone to leakage. Most of these mutations result in an abnormally short or malformed malcavernin protein that does not function. A shortage of this protein likely impairs the function of the complex. As a result, RhoA-GTPase signaling is turned on abnormally, weakening cellular junctions and increasing the permeability of blood vessel walls. The increased leakage into the brain can cause health problems such as headaches, seizures, and bleeding in the brain (cerebral hemorrhage) in some people with cerebral cavernous malformations.

Mutations in the CCM2 gene are involved in approximately 15 percent of all familial cerebral cavernous malformation cases.

Chromosomal Location

Cytogenetic Location: 7p13, which is the short (p) arm of chromosome 7 at position 13

Molecular Location: base pairs 44,999,746 to 45,076,470 on chromosome 7 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- C7orf22
- CCM2_HUMAN
- cerebral cavernous malformation 2
- chromosome 7 open reading frame 22
- MGC4067
- MGC4607
- OSM

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database (2000): Modulation of Barrier Function by Rho GTPases
<https://www.ncbi.nlm.nih.gov/books/NBK6487/#A36981>

GeneReviews

- Familial Cerebral Cavernous Malformation
<https://www.ncbi.nlm.nih.gov/books/NBK1293>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CCM2%5BALL%5D%29+OR+%28cerebral+cavernous+malformation+2%5BALL%5D%29+OR+%28CCM2+gene%5BALL%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- CCM2 GENE
<http://omim.org/entry/607929>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_CCM2.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=CCM2%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=21708
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/83605>
- UniProt
<http://www.uniprot.org/uniprot/Q9BSQ5>

Sources for This Summary

- OMIM: CCM2 GENE
<http://omim.org/entry/607929>
- Craig HD, Günel M, Cepeda O, Johnson EW, Ptacek L, Steinberg GK, Ogilvy CS, Berg MJ, Crawford SC, Scott RM, Steichen-Gersdorf E, Sabroe R, Kennedy CT, Mettler G, Beis MJ, Fryer A, Awad IA, Lifton RP. Multilocus linkage identifies two new loci for a mendelian form of stroke, cerebral cavernous malformation, at 7p15-13 and 3q25.2-27. *Hum Mol Genet.* 1998 Nov;7(12):1851-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9811928>
- Denier C, Goutagny S, Labauge P, Krivosic V, Arnoult M, Cousin A, Benabid AL, Comoy J, Frerebeau P, Gilbert B, Houtteville JP, Jan M, Lapierre F, Loiseau H, Menei P, Mercier P, Moreau JJ, Niveton-Chevallier A, Parker F, Redondo AM, Scarabin JM, Tremoulet M, Zerah M, Maciazeck J, Tournier-Lasserve E; Société Française de Neurochirurgie. Mutations within the MGC4607 gene cause cerebral cavernous malformations. *Am J Hum Genet.* 2004 Feb;74(2):326-37. Epub 2004 Jan 22.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14740320>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1181930/>

- Dupré N, Verlaan DJ, Hand CK, Laurent SB, Turecki G, Davenport WJ, Acciarri N, Dichgans J, Ohkuma A, Siegel AM, Rouleau GA. Linkage to the CCM2 locus and genetic heterogeneity in familial cerebral cavernous malformation. *Can J Neurol Sci.* 2003 May;30(2):122-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12774951>
- Liquori CL, Berg MJ, Siegel AM, Huang E, Zawistowski JS, Stoffer T, Verlaan D, Balogun F, Hughes L, Leedom TP, Plummer NW, Cannella M, Maglione V, Squitieri F, Johnson EW, Rouleau GA, Ptacek L, Marchuk DA. Mutations in a gene encoding a novel protein containing a phosphotyrosine-binding domain cause type 2 cerebral cavernous malformations. *Am J Hum Genet.* 2003 Dec;73(6):1459-64. Epub 2003 Nov 17.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14624391>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180409/>
- Liquori CL, Berg MJ, Squitieri F, Leedom TP, Ptacek L, Johnson EW, Marchuk DA. Deletions in CCM2 are a common cause of cerebral cavernous malformations. *Am J Hum Genet.* 2007 Jan; 80(1):69-75. Epub 2006 Nov 14.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17160895>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1785317/>
- Plummer NW, Zawistowski JS, Marchuk DA. Genetics of cerebral cavernous malformations. *Curr Neurol Neurosci Rep.* 2005 Sep;5(5):391-6. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16131422>
- Seker A, Pricola KL, Guclu B, Ozturk AK, Louvi A, Gunel M. CCM2 expression parallels that of CCM1. *Stroke.* 2006 Feb;37(2):518-23. Epub 2005 Dec 22.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16373645>
- Stockton RA, Shenkar R, Awad IA, Ginsberg MH. Cerebral cavernous malformations proteins inhibit Rho kinase to stabilize vascular integrity. *J Exp Med.* 2010 Apr 12;207(4):881-96. doi: 10.1084/jem.20091258. Epub 2010 Mar 22.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20308363>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2856024/>
- Verlaan DJ, Laurent SB, Rochefort DL, Liquori CL, Marchuk DA, Siegel AM, Rouleau GA. CCM2 mutations account for 13% of cases in a large collection of kindreds with hereditary cavernous malformations. *Ann Neurol.* 2004 May;55(5):757-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15122722>
- Whitehead KJ, Chan AC, Navankasattusas S, Koh W, London NR, Ling J, Mayo AH, Drakos SG, Jones CA, Zhu W, Marchuk DA, Davis GE, Li DY. The cerebral cavernous malformation signaling pathway promotes vascular integrity via Rho GTPases. *Nat Med.* 2009 Feb;15(2):177-84. doi: 10.1038/nm.1911. Epub 2009 Jan 18. Erratum in: *Nat Med.* 2009 Apr;15(4):462. Jones, Christopher A [added]; Zhu, Weiquan [added].
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19151728>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2767168/>
- Zawistowski JS, Stalheim L, Uhlik MT, Abell AN, Ancrile BB, Johnson GL, Marchuk DA. CCM1 and CCM2 protein interactions in cell signaling: implications for cerebral cavernous malformations pathogenesis. *Hum Mol Genet.* 2005 Sep 1;14(17):2521-31. Epub 2005 Jul 21.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16037064>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/CCM2>

Reviewed: November 2012

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications

U.S. National Library of Medicine

National Institutes of Health

Department of Health & Human Services